

been described for diabetes and hypertension; however, we are the first to provide proof of concept for its use in aging. We report that GMP-A increases circulating levels of Ang(1-7) when orally-administered over 4 weeks in aged F344/BN rats. Ongoing experiments examine GMP-A impact on distal tissues (muscle/brain). GMP-A provides translational advantages including ease of administration, production cost, and burden for regulatory approval.

#### THE INFLUENCE OF LIFE-EXTENDING MUTATION AND DIETARY INTERVENTION ON GUT MICROBIOTA

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The gastrointestinal microbiota represents a large and complex ecological system of different microorganisms. Recently, there is an increasing interest in the impact of microbiota on development of different age-related diseases. We tested the changes of gut microbiota during development in long-living Ames dwarf (df/df) mice and we compared the effects of this life-extending mutation with the impact of calorie restriction (CR). Importantly, the analysis of microbiome showed significant differences in the ratio of Bacteroidetes and Firmicutes when comparing df/df and normal (N) mice ( $p < 0.001$ ). The LefSe analysis showed distinct microbiome distribution between CR and ad libitum (AL) feeding regimen in N animals ( $p < 0.004$ ), yet there was lack of similar changes in response to CR in df/df mice. In summary, our study showed significant genotype impact on gut microbiota and we showed that life-extending CR regimen provide divergent effects on gut microbiota in N when comparing with df/df mice.

#### NONHUMAN PRIMATE GUT MICROBIOME: IMPACT OF AGE AND CALORIE RESTRICTION

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The human microbiome is composed of bacteria, archaea, viruses and eukaryotic microbes that reside in and on our bodies, the largest community of which is in the gut. Although the functions of the gut microbiota are not fully understood, they are known to play an essential role in immune, endocrine, and metabolic functions. To begin to understand the relationship between the gut microbiome, aging, and adult-onset, moderate calorie restriction in rhesus macaques (*Macaca mulatta*), we collected fecal samples at one timepoint from a total of 52 macaques for 16S rRNA gene analyses. Samples were taken from 20 males and 20 females across the natural macaque age range and from 6 males and 6 females enrolled in the long-term study of aging and calorie restriction at the Wisconsin National Primate Research Center. Preliminary data show that, like humans, NHPs exhibit a large interindividual variation in microbiota composition despite well-controlled environmental conditions.

## SESSION LB935 (LATE BREAKING POSTER)

### LATE BREAKING POSTER SESSION I

#### USING NEURAL NETWORK TO UNCOVER CELL TYPES THROUGH SNRNA SEQUENCING

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The advent of single-nucleus RNA-sequencing (snRNAseq) has allowed for the exploration of genetic signatures of the numerous cells in the brain. In particular, snRNAseq data can provide new insights into how many neurodegenerative diseases, such as Alzheimer's Disease, alter cells in the brain. One major challenge with analyzing snRNAseq data is the lack of a systematic way to classify the various cell types across different datasets. To address this challenge, we developed a general classifier ("DeepSeq") that uses state-of-the-art deep learning approaches. We trained our model on multiple snRNAseq datasets derived from post-mortem brain tissue in individuals with and without clinical diagnosis of Alzheimer's Disease from the ROSMAP cohorts. The two snRNAseq datasets contained 70,064 nuclei and 170,275 nuclei. The two studies employed different clustering techniques, and identified 44 and 18 putative cell types. To map these disparate cluster identities across datasets, we extracted the most relevant genes and trained two separate networks, one on each dataset. We then validated each classifier separately on the holdout cells. The resulting classifier accuracy were 87% and 94%. To map clusters across datasets, we then applied each classifier to the other dataset. Both classifiers yielded mappings that reflected the overall biology, correctly categorizing the nuclei into broad and fine cell type classes. Although validation on additional datasets would expand the generality of this approach, our results show that DeepSeq is an easily implementable classification tool that can assign identity to nuclei in new snRNAseq datasets without the need for preprocessing or cross-batch alignment.

#### PATHOLOGICAL TAU ABORTS CELL CYCLE ACTIVATION BY MIMICKING EPITHELIAL-MESENCHYMAL-TRANSITION IN NEURONS

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Alzheimer's disease (AD) is an irreversible neurodegenerative disorder which is characterized by neurofibrillary tau tangles and amyloid- $\beta$  plaques. Our laboratory uses tau transgenic *Drosophila* to rapidly test hypotheses along with human brain samples in order to ensure that our work is relevant to clinical endeavors. Using this approach, we identified a neurodegenerative pathway whereby pathological tau over-stabilizes filamentous actin (f-actin), leading to disrupting aberrant nuclear pleomorphisms and decondensation of heterochromatic DNA. Due to the neuronal phenotypes observed in tau-transgenic *Drosophila* and reentry of post-mitotic neurons into the cell cycle, we